SEQUENCE LISTING

<110> OHARA, Osamu NAGASE, Takahiro OISHI, Michio YOKOTA, Hiroshi KAMIDA, Osamu

<120> Gene encoding a guanine nucleotide exchange factor and the gene product thereof

<130> 3190-100

<140> US Unassigned

<141> 2006-09-28

<150> PCT/JP2005/005918

<151> 2005-03-29

<150> JP P2004-106268

<151> 2004-03-31

<160> 27

<170> Patentln version 3.1

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<213> Homo sopiens

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<223> Polynucleotide encoding the protein (SEQ ID NO:2) that have a function of guanine nucleotide exchange factor.

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Gln Glu Arg Pro Val Ser Leu Thr Ser Thr Thr Ser Ser Ser Gly Ser
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Ser Ser Ser Trp Leu Asn Val Lys Gly Pro Leu Ser Pro Phe Asn Ser 65 70 75 80

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Leu Lys Pro Val Gln Arg lle Leu Lys Tyr His Leu Leu Gln Glu

230

235

240

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Asp Ala lle Asp Thr Met Thr Cys Val Ala Trp Tyr lle Asn Asp Met 260 265 270

Lys Arg Arg His Glu His Ala Val Arg Leu Gln Glu Ile Gln Ser Leu 275 280 285

Leu lle Asn Trp Lys Gly Pro Asp Leu Thr Thr Tyr Gly Glu Leu Vol 290 295 300

Leu Glu Gly Thr Phe Arg Val His Arg Val Arg Asn Glu Arg Thr Phe 305 310 315 320

Phe Leu Phe Asp Lys Thr Leu Leu lle Thr Lys Lys Arg Gly Asp His 325 330 335

Phe Val Tyr Lys Gly Asn lle Pro Cys Ser Ser Leu Met Leu lle Glu 340 345 350

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Lys Gln Gln Tyr Ser lle Gln Ala Lys Thr Val Glu Glu Lys Arg Asn 370 375 380

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Glu Glu Glu Glu Glu Glu Glu Glu Glu Ser Leu Ala Val Ala Glu Gln 545 550 555 560

Val Ala Asp Phe Ala Ser Ser Leu Leu Ala Ala Leu His Cys Trp His 565 570 575

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Ser Pro Thr Ser Thr Glu Lys Arg Met Ser Phe Glu Ser Ile Ser Ser 610 615 620

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Phe Ser Ala Val Glu Gly Pro Ser Ala Glu Glu Thr Pro Ser Asp Thr 645 650 655

Glu Ser Pro Glu Val Leu Glu Thr Gln Leu Asp Ala His Gln Gly Leu 660 665 670

Leu Gly Met Asp Pro Pro Gly Asp Met Val Asp Phe Val Ala Ala Glu 675 680 685

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Gln Leu Met Ala Gln Glu His Ser Pro Pro Lys Pro Ser Ser Ala 1115 1120 1125

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1130 1135 1140

Ser Gln Arg Thr Thr Ser Pro Gly Gly Arg Pro Ser Ala Trp Ser 1145 1150 1155

Pro Leu Ser Pro Thr Glu Thr Phe Ser Trp Pro Asp Val Arg Glu 1160 1165 1170

Leu Cys Ser Lys Tyr Ala Ser Arg Asp Glu Ala Arg Arg Ala Gly 1175 1180 1185

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<213> Homo sapiens

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<222> (1)..(1095)

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3	Lys His Ser Lys	3 3 3	agc atc cag gcc lle Gln Ala Lys 285	aag 864
3 3 3 3 3	ag aaa cgg aac t Lys Arg Asn Trp 295	Thr His His Ile L	atc aag agg ctc ys Arg Leu IIe 300	atc 912

cta gag aac cac cat gcc acc att ccc cag aag gcc aag gaa gcc atc 960 Leu Glu Asn His His Ala Thr lle Pro Gln Lys Ala Lys Glu Ala lle 310 315 320 305 1008 ttg goo otg got too tot tot occ oot ogg too ogc tgo ogc oco gog Leu Glu Met Asp Ser Tyr Tyr Pro Asn Arg Tyr Arg Cys Ser Pro Glu 325 330 335 1056 cga cta and and act tag tee tee caa got gag ata tee ace ant ata Arg Leu Lys Lys Ala Trp Ser Ser Gln Asp Glu Val Ser Thr Asn Val 350 340 345 cgc cag gag cgc cgg caa tet gag cca acc aaa cac etg 1095 Arg Gln Gly Arg Arg Gln Ser Glu Pro Thr Lys His Leu 355 360 365 <210> 4 <211> 365 <212> PRT <213> Homo sapiens <400> 4 Lys Leu Ser Tyr Leu Gly Arg Val Val Arg Glu lle Val Glu Thr Glu 5 15 10 Arg Met Tyr Val Gln Asp Leu Arg Ser Ile Val Glu Asp Tyr Leu Leu 25 20 30 Lys lle lle Asp Thr Pro Gly Leu Leu Lys Pro Glu Gln Val Ser Ala 35 40 45

Leu Phe Gly Asn Ile Glu Asn Ile Tyr Alo Leu Asn Ser Gln Leu Leu

50 55 60

Arg Asp Leu Asp Ser Cys Asn Ser Asp Pro Val Ala Val Ala Ser Cys 65 70 75 80

Phe Val Glu Arg Ser Gln Glu Phe Asp lle Tyr Thr Gln Tyr Cys Asn 85 90 95

Asn Tyr Pro Asn Ser Val Ala Ala Leu Thr Glu Cys Met Arg Asp Lys 100 105 110

Gln Gln Alo Lys Phe Phe Arg Asp Arg Gln Glu Leu Leu Gln His Ser 115 120 125

Leu Pro Leu Gly Ser Tyr Leu Leu Lys Pro Val Gln Arg lle Leu Lys 130 135 140

Tyr His Leu Leu Gln Glu lle Alo Lys His Phe Asp Glu Glu Glu 145 150 155 160

Asp Gly Phe Glu Val Val Glu Asp Ala IIe Asp Thr Met Thr Cys Val 165 170 175

Ala Trp Tyr lle Asn Asp Met Lys Arg Arg His Glu His Ala Val Arg 180 185 190

Leu Gln Glu IIe Gln Ser Leu Leu IIe Asn Trp Lys Gly Pro Asp Leu 195 200 205 Thr Thr Tyr Gly Glu Leu Vol Leu Glu Gly Thr Phe Arg Vol His Arg 210 215 220

Val Arg Asn Glu Arg Thr Phe Phe Leu Phe Asp Lys Thr Leu Leu Ile
225 230 235 240

Thr Lys Lys Arg Gly Asp His Phe Val Tyr Lys Gly Asn lle Pro Cys 245 250 255

Ser Ser Leu Met Leu IIe Glu Ser Thr Arg Asp Ser Leu Cys Phe Thr 260 265 270

Val Thr His Tyr Lys His Ser Lys Gln Gln Tyr Ser lle Gln Ala Lys 275 280 285

Thr Vol Glu Glu Lys Arg Asn Trp Thr His His IIe Lys Arg Leu IIe 290 295 300

Leu Glu Asn His His Ala Thr lle Pro Gln Lys Ala Lys Glu Ala lle 305 310 315 320

Leu Glu Met Asp Ser Tyr Tyr Pro Asn Arg Tyr Arg Cys Ser Pro Glu 325 330 335

Arg Leu Lys Lys Ala Trp Ser Ser Gln Asp Glu Val Ser Thr Asn Val 340 345 350

Arg Gln Gly Arg Arg Gln Ser Glu Pro Thr Lys His Leu

355

360

365

<210> 5

<211> 1102

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<223> Polynucleotide having kozak consensus sequence and methionine codon in its 5'-terminal, followed by partial sequence of SEQ ID NO:1 of the 581st to 1675th nucleotides having a region encoding DbI homology domain and Pleckstrin homology domain, encoding SEQ ID NO:6.

<220>

<221> CDS

<222> (5)..(1102)

<220>

<221> misc_feature

<222> (1)..(4)

<223> kozak consensus sequence

<220>

<221> misc_feature

<222> (5)..(7)

<223> methionine codon

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cacc atg aag ctc agc tac ctg ggc cga gtg gtg cgg gag atc gtg gag Met Lys Leu Ser Tyr Leu Gly Arg Val Val Arg Glu lie Val Glu

1

5

10

15

oco gag cgc atg tac gta cag gac ctg cgc agc atc gtg gag gac tac Thr Glu Arg Met Tyr Val Gln Asp Leu Arg Ser Ile Val Glu Asp Tyr 20 25 30	97
ctc ttg aag atc att gac aca ccc ggg ctg ctg aag cca gaa cag gtc Leu Leu Lys IIe IIe Asp Thr Pro Gly Leu Leu Lys Pro Glu Gln Val 35 40 45	145
agc gcc ctc ttt ggg aac ata gaa aac atc tac gcg ctg aac agc cag Ser Ala Leu Phe Gly Asn IIe Glu Asn IIe Tyr Ala Leu Asn Ser Gln 50 55 60	193
ctc ctc aga gac ctg gac agc tgc aat agt gac ccc gtg gct gtg gcc Leu Leu Arg Asp Leu Asp Ser Cys Asn Ser Asp Pro Val Ala Val Ala 65 70 75	241
agc tgc ttt gtg gaa agg agc caa gag ttt gat atc tac act cag tat Ser Cys Phe Val Glu Arg Ser Gln Glu Phe Asp lle Tyr Thr Gln Tyr 80 85 90 95	289
tgc aac aat tac ccc aac tcc gtg gcc gcc ctg acg gaa tgc atg cgg Cys Asn Asn Tyr Pro Asn Ser Val Ala Ala Leu Thr Glu Cys Met Arg 100 105 110	337
gac aag cag cag gcc aag ttc ttt cgg gac cgg cag gag ctg cta cag Asp Lys Gln Gln Ala Lys Phe Phe Arg Asp Arg Gln Glu Leu Leu Gln 115 120 125	385
cac tog otg occ ttg ggo toc tac otg otg aag oca gto oag ogc ato His Ser Leu Pro Leu Gly Ser Tyr Leu Leu Lys Pro Val Gln Arg lle 130 135 140	433
ctc aag tac cac ctg ctg ctc cag gaa att gcc aaa cat ttt gat gaa Leu Lys Tyr His Leu Leu Leu Gln Glu IIe Ala Lys His Phe Asp Glu 145 150 155	481
gaa gag gat ggc ttt gag gtg gtg gag gat gcc att gac acc atg acc	529

Glu Glu Asp Gly Phe Glu Val Val Gl 160 165	lu Asp Ala IIe Asp Thr Met Thr 170 175	
tgt gtg gcc tgg tac atc aac gac o Cys Val Ala Trp Tyr lle Asn Asp Me 180	atg aag agg agg cat gag cac gcg et Lys Arg Arg His Glu His Ala 185 190	577
gtc cgg ctc cag gag att cag tca Val Arg Leu Gin Glu IIe Gin Ser Le 195	** * * * * * * * * * * * * * * * * * * *	625
goc ctg acc acc tac ggg gag ctt Asp Leu Thr Thr Tyr Gly Glu Leu V 210 215	'al Leu Glu Gly Thr Phe Arg Val	673
cat cgc gtg cgc aat gao agg acc His Arg Val Arg Asn Glu Arg Thr P 225 230		721
ctt atc acc aag aag cgg ggc gat Leu lle Thr Lys Lys Arg Gly Asp Hi 240 245		769
ccg tgc tcc tcc ctg atg ctg atc g Pro Cys Ser Ser Leu Met Leu IIe (260		817
ttc act gtc acc cac tac aag cac Phe Thr Val Thr His Tyr Lys His Se 275	agc aag cag cag tac agc atc cag er Lys Gln Gln Tyr Ser IIe Gln 280 285	865
gcc aag aca gtg gag gag aaa cga Ala Lys Thr Val Glu Glu Lys Arg As 290 295		913
ctc atc cta gag aac coc cat gcc Leu IIe Leu Glu Asn His His Ala Th 305 310	acc att ccc cag aag gcc aag gaa or lle Pro Gln Lys Ala Lys Glu 315	961

gcc atc ttg gao atg gat tcc tat tot ccc aat cgg tac cgc tgc agc 1009 Ala lle Leu Glu Met Asp Ser Tyr Tyr Pro Asn Arg Tyr Arg Cys Ser 335 320 325 330 cco gag cgg ctg and and gct tgg tcc tcc cag gat gag gtg tcc acc 1057 Pro Glu Arg Leu Lys Lys Ala Trp Ser Ser Gln Asp Glu Val Ser Thr 350 340 345 aat gtg cgc cag ggg cgc cgg caa tct gag cca acc aaa cac ctg 1102 Asn Vol Arg Gln Gly Arg Arg Gln Ser Glu Pro Thr Lys His Leu 355 360 <210> 6 <211> 366 <212> PRT <213> Homo sapiens <400> 6 Met Lys Leu Ser Tyr Leu Gly Arg Val Val Arg Glu lle Val Glu Thr 15 10 Glu Arg Met Tyr Val Gln Asp Leu Arg Ser Ile Val Glu Asp Tyr Leu 20 25 30 Leu Lys IIe IIe Asp Thr Pro Gly Leu Leu Lys Pro Glu Gln Val Ser 40 45 35 Alo Leu Phe Gly Asn Ile Glu Asn Ile Tyr Alo Leu Asn Ser Gln Leu

Leu Arg Asp Leu Asp Ser Cys Asn Ser Asp Pro Val Ala Val Ala Ser

60

55

65 70 75 80

Cys Phe Val Glu Arg Ser Gln Glu Phe Asp lle Tyr Thr Gln Tyr Cys 85 90 95

Asn Asn Tyr Pro Asn Ser Val Ala Ala Leu Thr Glu Cys Met Arg Asp 100 105 110

Lys Gln Gln Ala Lys Phe Phe Arg Asp Arg Gln Glu Leu Leu Gln His
115
120
125

Ser Leu Pro Leu Gly Ser Tyr Leu Leu Lys Pro Val Gln Arg Ile Leu 130 135 140

Lys Tyr His Leu Leu Gln Glu lle Alo Lys His Phe Asp Glu Glu
145 150 155 160

Glu Asp Gly Phe Glu Val Val Glu Asp Ala lle Asp Thr Met Thr Cys 165 170 175

Val Ala Trp Tyr Ile Asn Asp Met Lys Arg Arg His Glu His Ala Val 180 185 · 190

Arg Leu Gln Glu Ile Gln Ser Leu Leu Ile Asn Trp Lys Gly Pro Asp 195 200 205

Leu Thr Thr Tyr Gly Glu Leu Val Leu Glu Gly Thr Phe Arg Val His 210 215 220

Arg Val Arg Asn Glu Arg Thr Phe Phe Leu Phe Asp Lys Thr Leu Leu lle Thr Lys Lys Arg Gly Asp His Phe Val Tyr Lys Gly Asn lle Pro Cys Ser Ser Leu Met Leu IIe Glu Ser Thr Arg Asp Ser Leu Cys Phe Thr Val Thr His Tyr Lys His Ser Lys Gln Gln Tyr Ser lle Gln Ala Lys Thr Vol Glu Glu Lys Arg Asn Trp Thr His His Ile Lys Arg Leu lle Leu Glu Asn His His Ala Thr lle Pro Gln Lys Ala Lys Glu Ala lle Leu Glu Met Asp Ser Tyr Tyr Pro Asn Arg Tyr Arg Cys Ser Pro Glu Arg Leu Lys Lys Ala Trp Ser Ser Gln Asp Glu Val Ser Thr Asn Vol Arg Gln Gly Arg Arg Gln Ser Glu Pro Thr Lys His Leu

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34

caccatgoog ctcagctacc tgggccgagt ggtg

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<220>		
	Designed polynucleotide based on the sequence of SEQ ID NO:1 use as a primer	for
<400>	10	
caggtgtt	tg gttggctcag attgcc	26
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	Artificial	
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t	t us a primer	
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	Artificial	
\2137	Artificial	
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	14	
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	DNA	
<213>	Artificial	
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\	a primer	U.C.
	о р	
<400>	14	
tcatago	agc acacacetge ggete	25
<210>	15	
<211>	29	
<212>	DNA	
<213>	Artificial	
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	a primer	-
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<220> <223>	Designed polynucleotide based on the sequence of RhoA for use a primer	OS
<400> tcacaag		28
<210><211><211><212><213>		
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<400>	17 gcag gccatcaagt gtgtggtgg	29
<210><211><211><212><213>	18 26 DNA Artificial	
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<400>	18	

ttocoocogc aggcatttc tcttcc	26
<210> 19 <211> 7 <212> DNA <213> ortificial	
<220> <223> Designed oligonucleotide including Kozak consensus sequence wed by a methionine codon.	follo
<400> 19 caccatg	
<210> 20 <211> 576 <212> DNA <213> homo sapiens <220> <221> misc_feature <223> Cdc42 gene	
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gcagtcacag ttatgattgg tggagaacca talactcttg gactttttga tactgcaggg	180

coogagatt atgacagatt acgaccacta agttatccac aaacagatat atttetagtc

tgttttcag tggtctctcc atcttcattt gaaaacgtga aagaaaagtg ggtgcctgag

ataactcacc actglccaaa gactcellte ligetiglig ggactcaaat igaleteaga

240

300

gatgacccct ctactattga gaaacttgcc aagaacaaac agaagcctat cactccagag 420
actgctgaaa agctggcccg tgacctgaag gctgtcaagt atgtggagtg ttctgcactt 480
acacagaaag gcctaaagaa tgtatttgac gaagcaatat tggctgccct ggagcctcca 540
gaaccgaaga agagccgcag gtgtgtgctg ctatga 576

<210> 21

<211> 191

<212> PRT

<213> homo sapiens

<220>

<221> misc_feature

<223> Cdc42

<400> 21

Met Gln Thr lle Lys Cys Val Val Val Gly Asp Gly Ala Val Gly Lys 1 5 10 15

Thr Cys Leu Leu Ile Ser Tyr Thr Thr Asn Lys Phe Pro Ser Glu Tyr 20 25 30

Val Pro Thr Val Phe Asp Asn Tyr Ala Val Thr Val Met IIe Gly Gly 35 40 45

Glu Pro Tyr Thr Leu Gly Leu Phe Asp Thr Ala Gly Gln Glu Asp Tyr 50 55 60

Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp Vol Phe Leu Vol 65 70 75 80

Cys Phe Ser Val Val Ser Pro Ser Ser Phe Glu Asn Val Lys Glu Lys 85 90 95

Trp Val Pro Glu lle Thr His His Cys Pro Lys Thr Pro Phe Leu Leu 100 105 110

Val Gly Thr Gln lle Asp Leu Arg Asp Asp Pro Ser Thr lle Glu Lys
115 120 125

Leu Ala Lys Asn Lys Gln Lys Pro lle Thr Pro Glu Thr Ala Glu Lys 130 135 140

Leu Ala Arg Asp Leu Lys Ala Val Lys Tyr Val Glu Cys Ser Ala Leu 145 150 155 160

Thr Gln Lys Gly Leu Lys Asn Val Phe Asp Glu Ala Ile Leu Ala Ala $16\overline{5}$ 170 175

Leu Glu Pro Pro Glu Pro Lys Lys Ser Arg Arg Cys Val Leu Leu 180 185 190

<210> 22

<211> 582

<212> DNA

<213> homo sopiens

<220>

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<210> 23

<211> 193

<212> PRT

<213> homo sapiens

<220>

<221> misc_feature

<223> RhoA

<400> 23

Met Ala Ala Ile Arg Lys Lys Leu Val Ile Val Gly Asp Gly Ala Cys Gly Lys Thr Cys Leu Leu Ile Val Phe Ser Lys Asp Gln Phe Pro Glu Val Tyr Val Pro Thr Val Phe Glu Asn Tyr Val Ala Asp lle Glu Val Asp Gly Lys Gln Val Glu Leu Ala Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Asp Thr Asp Val Ile Leu Met Cys Phe Ser lle Asp Ser Pro Asp Ser Leu Glu Asn lle Pro Glu Lys Trp Thr Pro Glu Val Lys His Phe Cys Pro Asn Val Pro Ile lle Leu Val Gly Asn Lys Lys Asp Leu Arg Asn Asp Glu His Thr Arg Arg Glu Leu Ala Lys Met Lys Gln Glu Pro Val Lys Pro Glu Glu Gly Arg Asp Met Ala Asn Arg IIe Gly Ala Phe Gly Tyr Met Glu Cys Ser

Ala Lys Thr Lys Asp Gly Val Arg Glu Val Phe Glu Met Ala Thr Arg 165 170 175

Ala Ala Leu Gln Ala Arg Arg Gly Lys Lys Lys Ser Gly Cys Leu Val 180 185 190

Leu

<210> 24

<211> 579

<212> DNA

<213> homo sapiens

<220>

<221> misc_feature

<223> Rac1 gene

<400> 24

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ataagttaca caaccaatga attaataa gaatatataa taatagaa taagataga 120

tagataata talagataga tagaanaaca galaatataga gataatagaa taagataga 180

caagaagatt atgacagatt aagacaacta taataacaa aanaagata gatataatt 240

tagattitaa tagaagata tagaanaata gaanaatata gaanaataga gaanaaga gaanaada gaanaata tagatataga 300

gatagataana aaagataana gaanaataana gaanaagaa taaataaaat taatataag 360

gatagataana aaaagataa gaanaataana gaanaagaaga taaataaaat taatataag 420

cagggtctag ccatggctaa ggagattggt gctgtaaaat acctggagtg ctcggcgctc 480
acacagcgag gcctcaagac agtgtttgac gaagcgatcc gagcagtcct ctgcccgcct 540
cccgtgaaga agaggaagag aaaatgcctg ctgttgtaa 579

<210> 25
<211> 192
<212> PRT
<213> homo sapiens

<220>
<221> misc_feature
<223> Rac1

<400> 25

Met Gln Ala lle Lys Cys Val Val Gly Asp Gly Ala Val Gly Lys
1 5 10 15

Thr Cys Leu Leu lle Ser Tyr Thr Thr Asn Alo Phe Pro Gly Glu Tyr 20 25 30

lle Pro Thr Val Phe Asp Asn Tyr Ser Ala Asri Val Met Val Asp Gly . $35 \hspace{1cm} 40 \hspace{1cm} 45$

Lys Pro Vol Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr 50 55 60

Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp Vol Phe Leu Ile 65 70 75 80 Cys Phe Ser Leu Val Ser Pro Ala Ser Phe Glu Asn Val Arg Ala Lys 85 90 95

Trp Tyr Pro Glu Val Arg His His Cys Pro Asn Thr Pro IIe IIe Leu 100 105 110

Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Asp Thr Ile Glu Lys 115 120 125

Leu Lys Glu Lys Lys Leu Thr Pro IIe Thr Tyr Pro Gln Gly Leu Ala 130 135 140

Met Ala Lys Glu lle Gly Ala Val Lys Tyr Leu Glu Cys Ser Ala Leu
145 150 155 160

Thr Gln Arg Gly Leu Lys Thr Vol Phe Asp Glu Ala lle Arg Ala Vol 165 170 175

Leu Cys Pro Pro Pro Val Lys Lys Arg Lys Arg Lys Cys Leu Leu Leu 180 185 190

<210> 26

<211> 3652

<212> DNA

<213> Homo sapiens

<220>

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<223> Gene encoding proto-Dbl (SEO ID NO:27)

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                                                                  120
catcoatgtt gcgttgocoo ttggooogga aaagtgtoot tgcgtacogg cgaa atg
                                                                      177
                                                             Met
                                                             1
gco gao gca aat ccc cgg aga ggc aag atg agg ttc aga agg aat gcg
                                                                        225
Ala Glu Ala Asn Pro Arg Arg Gly Lys Met Arg Phe Arg Arg Asn Ala
            5
                                 10
                                                     15
                                                                  273
get tee the eet ggg aac the eac the eth the egh eet acc
Ala Ser Phe Pro Gly Asn Leu His Leu Val Leu Val Leu Arg Pro Thr
        20
                             25
                                                 30
age til ett eaa ega aeg tie aea goe alt gga til tag til agt eag
                                                                   321
Ser Phe Leu Gln Arg Thr Phe Thr Asp Ile Gly Phe Trp Phe Ser Gln
    35
                                             45
                        40
gag got titl atg cct and the cca git git atg ctg age tea git agt
                                                                   369
Glu Asp Phe Met Pro Lys Leu Pro Val Val Met Leu Ser Ser Val Ser
50
                    55
                                         60
                                                              65
got ttg ctg aca tac att got goc aag caa tta acc cct gog tta ggc
                                                                     417
Asp Leu Leu Thr Tyr lle Asp Asp Lys Gln Leu Thr Pro Glu Leu Gly
                70
                                     75
                                                         80
ggc acc ttg cog tac tgc coc agt goa tgg atc atc ttc aga oat act
                                                                     465
Gly Thr Leu Gln Tyr Cys His Ser Glu Trp lle lle Phe Arg Asn Ala
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85	Ō	90	95		
,	t gcc ctc oca c e Ala Leu Thr V	•	3 3 3	3	513
	i gaa ctg gct g ir Glu Leu Ala (120	Glu Thr Glu Leu			561
•	na att ctg gca lle Leu Ala lle 135	Arg Ala Glu Ar	2 2		609
, ,	t aca gct gta d e Thr Ala Val Th 150	, ,	, ,		657
Asn Leu Glu Vo	g cct gac act o al Pro Asp Thr (65			eu Glu	705
3	a ata agt ggt g n Ile Ser Gly As		•		753
,	ot gat atg gaa Asp Met Glu T 200	hr Ala Phe Asp	33 33		801
	a atg gag cag s Met Glu Gln T 215	yr Leu Gln Lei			849
,	g ctt gtg act g in Leu Val Thr (230				897

gca gao ctg gct gat gta oca ggg oct ata gct caa gta ooa cao ooa Ala Glu Leu Ala Asp Val Thr Gly Thr IIe Ala Gln Val Lys Gln Lys 245 250 255	945
ata aaa aaa ttg gaa aac tta gat gaa aat tct cog gag cta tta tca Ile Lys Lys Leu Glu Asn Leu Asp Glu Asn Ser Gln Glu Leu Leu Ser 260 265 270	993
aag gcc cag ttt gtg ata tta cat gga cac aag ctt gca gca aat cac Lys Ala Gln Phe Val IIe Leu His Gly His Lys Leu Ala Ala Asn His 275 280 285	1041
cat tat gca ctt gat tta atc tgc cag agg tgc aat gag cta cgt tac His Tyr Ala Leu Asp Leu IIe Cys Gln Arg Cys Asn Glu Leu Arg Tyr 290 295 300 305	1089
ctt tct gat att ttg gtt aat gag ata aaa gca aaa cgg ata caa ctc Leu Ser Asp IIe Leu Val Asn Glu IIe Lys Ala Lys Arg IIe Gln Leu 310 315 320	1137
agc agg acc ttc aaa atg cat aaa ctc cta cag cag gct cgt caa tgc Ser Arg Thr Phe Lys Met His Lys Leu Leu Gln Gln Ala Arg Gln Cys 325 330 335	1185
tgt gat gaa ggg goa tgt ctt cta gct aat cag gaa ata gat oag ttt Cys Asp Glu Gly Glu Cys Leu Leu Ala Asn Gln Glu Ile Asp Lys Phe 340 345 350	1233
cog tot aaa gaa gat got cag aaa got oto caa gac att gaa aat ttt GIn Ser Lys GIu Asp Ala GIn Lys Ala Leu GIn Asp IIe GIu Asn Phe 355 360 365	1281
ctt gaa atg gct cta ccc ttt ata aat tat gaa cct gaa aca ctg cag Leu Glu Met Ala Leu Pro Phe IIe Asn Tyr Glu Pro Glu Thr Leu Gln 370 375 380 385	1329
tot gaa tit gat gta ota tia tot oot gag oit aag git oaa atg aag Tyr Glu Phe Asp Val IIe Leu Ser Pro Glu Leu Lys Val Gln Met Lys	1377

	390	395	400	0
	c aag ett gaa aac Lys Leu Glu Asn 5	, ,	3 3	cag 1425
3 3 33	agg aoc ctg gcc Arg Asn Leu Ala 42	Asp Lys His	0 0 00	
3 3 3	aca cct gao aat Thr Pro Glu Asn 440	3 3	3 3 3	
	caa ggg aag aag s GIn GIy Lys Lys 455	33 3	Gln Asn Gln Ser As	
-	o gtg gtg cct gat Val Val Pro Asp (470	2 2 2 2	, , ,	1
-	t ttg gac aat ggc r Leu Asp As'n Gly :5			
•	t gaa ctg ata cag n Glu Leu IIe GIn ⁵ 50	Thr Glu Arg Vo	-	goo 1713
-	ttg ttg ggt tat ag Leu Leu Gly Tyr 520		•	-
	atg cca cct ctc c eu Met Pro Pro Le 535		n Lys Lys Asp lle	

ttt gga aac atg gca gaa at Phe Gly Asn Met Ala Glu Ile 550	•	-	1857
agc agc ctg gaa aat tgt gc Ser Ser Leu Glu Asn Cys Ald 565			1905
ttc ctg gaa agg aag gat go Phe Leu Glu Arg Lys Asp As 580			1953
aat aag ccc aga tca gaa a Asn Lys Pro Arg Ser Glu Th 595 6	55 55 5	er Glu Cys Ala	2001
ttt ttc cag gaa tgt caa aga Phe Phe GIn Glu Cys GIn Ar 610 615	•		2049
tcc tat tta ctc aao cca gtg Ser Tyr Leu Leu Lys Pro Va 630	,	•	2097
ttg aag gag cta tta aoo ta Leu Lys Glu Leu Leu Lys Ty 645			2145
ttg aag aag gca ctc gat gc Leu Lys Lys Ala Leu Asp Ala 660	*		2193
gat tot atg cat cag att god Asp Ser Met His GIn IIe Ala 675 6		Asn Leu Asn	2241
gaa ctg ggc aag atg ata a Glu Leu Gly Lys Met Ile Met			2289

690	695	700		705
•	ggt gct aca aaa at y Ala Thr Lys Met 710		•	ca 2337
Met Gln Arg H	cac ctt ttc ttg tat o is Leu Phe Leu Tyr 25	-	-	. 2385
	aa agt gga gaa gg u Ser Gly Glu Gly S 74	Ser Asp Arg Tyr I		gt 2433
_	ıt tgg aca atg gat ys Trp Lys Met Asp 760	Glu Val Gly lle	-	2481
55 5	ac cgc aag ttt gad sn Arg Lys Phe Glu 775	33 30		785 2529
-	cog gct tct aat g Gln Ala Ser Asn Vo 790			2577
Lys Glu lle Arg	oga aat att ttg ttg g Asn IIe Leu Leu L 05			2625
-	aag caa cag gat c /s GIn GIn Asp GIn 82	Leu Thr Glu Arg		•
	g cag aat gat gaa n Gln Asn Asp Glu 840	Lys Gln Gln Gly	-	2721

act gag gao act gao ttg gao cac acc agc act gtg gtg gag gtc tgt Thr Glu Glu Thr Glu Leu Glu His Thr Ser Thr Val Val Glu Val Cys	2769
850 855 860 865	•
gag gco att gcg tca gtt cag gca gaa gca aat aca gtt tgg act gag Glu Ala IIe Ala Ser Val Gln Ala Glu Ala Asn Thr Val Trp Thr Glu 870 875 880	2817
gca tca caa tct gca gaa atc tct gaa gaa cct gcg gaa tgg tca agc Ala Ser Gln Ser Ala Glu lle Ser Glu Glu Pro Ala Glu Trp·Ser Ser 885 890 895	2865
aac tat ttc tac cct act tat gat gaa oot gaa gaa gaa oot ogg ccc Asn Tyr Phe Tyr Pro Thr Tyr Asp Glu Asn Glu Glu Glu Asn Arg Pro 900 905 910	2913
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Thr Ser Phe Leu Gln Arg Thr Phe Thr Asp Ile Gly Phe Trp Phe Ser 35 40 45

Gln Glu Asp Phe Met Pro Lys Leu Pro Vol Val Met Leu Ser Ser Val 50 55 60

Ser Asp Leu Leu Thr Tyr lle Asp Asp Lys Gln Leu Thr Pro Glu Leu 65 70 75 80

Gly Gly Thr Leu Gln Tyr Cys His Ser Glu Trp IIe IIe Phe Arg Asn 85 90 95

Ala Ile Glu Asn Phe Ala Leu Thr Val Lys Glu Met Ala Gln Met Leu Gln Ser Phe Gly Thr Glu Leu Alo Glu Thr Glu Leu Pro Asp Asp Ile Pro Ser Ile Glu Glu Ile Leu Ala Ile Arg Ala Glu Arg Tyr His Leu Leu Lys Asn Asp lle Thr Ala Val Thr Lys Glu Gly Lys lle Leu Leu Thr Asn Leu Glu Val Pro Asp Thr Glu Gly Ala Val Ser Ser Arg Leu Glu Cys His Arg Gln Ile Ser Gly Asp Trp Gln Thr Ile Asn Lys Leu Leu Thr Gln Val His Asp Mei Glu Thr Ala Phe Asp Gly Phe Trp Glu Lys His Gln Leu Lys Met Glu Gln Tyr Leu Gln Leu Trp Lys Phe Glu Gln Asp Phe Gln Gln Leu Val Thr Glu Val Glu Phe Leu Leu Asn Gln

Gln Ala Glu Leu Ala Asp Val Thr Gly Thr Ile Ala Gln Val Lys Gln

Lys lle Lys Lys Leu Glu Asn Leu Asp Glu Asn Ser Gln Glu Leu Leu Ser Lys Ala Gln Phe Val IIe Leu His Gly His Lys Leu Ala Ala Asn His His Tyr Alo Leu Asp Leu lle Cys Gln Arg Cys Asn Glu Leu Arg Tyr Leu Ser Asp lle Leu Val Asn Glu lle Lys Ala Lys Arg lle Gln Leu Ser Arg Thr Phe Lys Met His Lys Leu Leu Gln Gln Ala Arg Gln Cys Cys Asp Glu Gly Glu Cys Leu Leu Ala Asn Gln Glu lle Asp Lys Phe Gln Ser Lys Glu Asp Ala Gln Lys Ala Leu Gln Asp lle Glu Asn Phe Leu Glu Met Ala Leu Pro Phe Ile Asn Tyr Glu Pro Glu Thr Leu Gln Tyr Glu Phe Asp Val IIe Leu Ser Pro Glu Leu Lys Val Gln Met

Lys Thr IIe Gln Leu Lys Leu Glu Asn IIe Arg Ser IIe Phe Glu Asn Gln Gln Ala Gly Phe Arg Asn Leu Ala Asp Lys His Val Arg Pro Ile Gln Phe Val Val Pro Thr Pro Glu Asn Leu Val Thr Ser Gly Thr Pro Phe Phe Ser Ser Lys Gln Gly Lys Lys Thr Trp Arg Gln Asn Gln Ser Asn Leu Lys lle Glu Val Val Pro Asp Cys Gln Glu Lys Arg Ser Ser Gly Pro Ser Ser Leu Asp Asn Gly Asn Ser Leu Asp Vol Leu Lys Asn His Val Leu Asn Glu Leu IIe Gln Thr Glu Arg Val Tyr Val Arg Glu Leu Tyr Thr Val Leu Leu Gly Tyr Arg Ala Glu Met Asp Asn Pro Glu Met Phe Asp Leu Met Pro Pro Leu Leu Arg Asn Lys Lys Asp lle Leu Phe Gly Asn Met Ala Glu lle Tyr Glu Phe His Asn Asp lle Phe Leu Ser Ser Leu Glu Asn Cys Ala His Ala Pro Glu Arg Val Gly Pro 565 570 575

Cys Phe Leu Glu Arg Lys Asp Asp Phe Gln Met Tyr Ala Lys Tyr Cys 580 585 590 .

Gln Asn Lys Pro Arg Ser Glu Thr Ile Trp Arg Lys Tyr Ser Glu Cys 595 600 605

Ala Phe Phe Gln Glu Cys Gln Arg Lys Leu Lys His Arg Leu Arg Leu 610 615 620

Asp Ser Tyr Leu Leu Lys Pro Val Gln Arg lle Thr Lys Tyr Gln Leu 625 630 635 640

Leu Leu Lys Glu Leu Leu Lys Tyr Ser Lys Asp Cys Glu Gly Ser Alo 645 650 655

Leu Leu Lys Lys Ala Leu Asp Ala Met Leu Asp Leu Leu Lys Ser Val 660 665 670

Asn Asp Ser Met His Gln IIe Alo IIe Asn Gly Tyr IIe Gly Asn Leu 675 680 685

Asn Glu Leu Gly Lys Met lle Met Gln Gly Gly Phe Ser Vol Trp lle 690 695 700

Gly His Lys Lys Gly Ala Thr Lys Met Lys Asp Leu Ala Arg Phe Lys Pro Met Gln Arg His Leu Phe Leu Tyr Glu Lys Ala lle Val Phe Cys Lys Arg Arg Val Glu Ser Gly Glu Gly Ser Asp Arg Tyr Pro Ser Tyr Ser Phe Lys His Cys Trp Lys Met Asp Glu Val Gly Ile Thr Glu Tyr Val Lys Gly Asp Asn Arg Lys Phe Glu lle Trp Tyr Gly Glu Lys Glu Glu Val Tyr lle Val Gln Ala Ser Asn Val Asp Val Lys Met Thr Trp Leu Lys Glu lle Arg Asn lle Leu Leu Lys Gln Gln Glu Leu Leu Thr Val Lys Lys Arg Lys Gln Gln Asp Gln Leu Thr Glu Arg Asp Lys Phe Gln lle Ser Leu Gln Gln Asn Asp Glu Lys Gln Gln Gly Ala Phe lle Ser Thr Glu Glu Thr Glu Leu Glu His Thr Ser Thr Val Val Glu Val

Cys Glu Ala IIe Ala Ser Val Gln Ala Glu Ala Asn Thr Val Trp Thr 865 870 875 880

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